59. (New claim) A method for the treatment of *Helicobacter* infection in a mammalian host comprising administering to the mammalian host an effective amount of the vaccine composition according to claim 58.

60. (New claim) A method for preventing or reducing the risk of *Helicobacter* infection in a mammalian host, comprising administering to the mammalian host an effective amount of the vaccine composition according to claim 58.

REMARKS

In compliance with 37 C.F.R.§§ 1.821-1.825 and in response to the Notice to Comply (copy enclosed) accompanying the Office Action, the Sequence Listing has been revised to define the sequences disclosed at pages 22-24 and 26 of the specification. Accordingly, the specification has been amended to insert the respective SEQ ID NO's for the sequences disclosed where appropriate. A paper copy of the revised Sequence Listing is enclosed with this Amendment to replace the Sequence Listing filed with the application. No new matter has been introduced by these amendments.

In compliance with 37 CFR §§ 1.821-1.825, enclosed is a revised computer readable copy of the Sequence Listing for this application. The content of the computer readable copy of the Sequence Listing submitted herewith is identical to that of the paper copy also provided herewith. Applicants assert that no new matter has been introduced in these submissions.

The Examiner has indicated, at page 3 of the Action, that Applicants use trademark names at page 15, lines 5-9 of the specification. According to the Examiner, the trademark names should be capitalized and accompanied by the generic terminology of the compounds in accordance with the rules. Applicants point out that the Examiner is in error. No trademark names are used in the cited disclosure at page 15 of the specification. The capitalized terms are well known acronyms for the full chemical names of the compounds defined within the brackets following each term.

The specification has also been amended at page 12 to correct a typographical error and to define the acronym "ASES."

Claims 1-27, 29, 32-34, 36-38, 45-47 and 49-52 have been amended to more clearly define the invention with the particularity required by statute. Claims 39-44 have been canceled. New claims 53-60 have been added. Thus, upon entry of the amendments herein, claims 1-38, and 45-60 are pending in the application. New claims 53-57 are directed to the subject matter deleted from original, improper multiple-dependent claim 22. New claims 58-60 are directed to the subject matter deleted from original, improper multiple dependent claims 50-52.

The Examiner has objected to claims 4-8, 11-37, and 45-52 under 37 C.F.R. § 1.75(c), because they are written in improper multiple dependent form. The claims have been amended, and they are now in proper form.

Claims 51 and 52 were rejected under 35 U.S.C. § 112. The Examiner alleges that the claims are indefinite because they recite the use of the claimed delivery system, and the claim does not set forth any steps involved. The Examiner has also rejected claims 51 and 52 under 35 U.S.C. § 101 because they recite non-statutory subject matter. Claims 51 and 52 have been amended, and, as amended, they overcome these rejections.

Claims 38-44 have been rejected under 35 U.S.C. § 112, first paragraph. According to the Examiner, claims 38-44 are being read as vaccine claims, because the recitation of the word "vaccine" defines the protein in the delivery system as the protective antigen, and not the polymer particles. Based on this interpretation, the Examiner has rejected the claims and alleges that the specification is enabling for a method of making polymer particles that comprises a protein or a lipoprotein. According to the Examiner, the specification does not provide enablement for vaccines comprising any protein from any source or any *Helicobacter* protein from any species or any fragment of *Helicobacter* protein as claimed. It is the Examiner's position that the specification contains no evidence showing that any polymer particle comprising any protein or fragment of the protein could confer the desired and claimed protective immunity. Applicants disagree.

Claims 39-44 have been canceled. Therefore, the rejection of these claims is now moot. Claim 38 has been amended to more clearly recite the invention. Support for amended claim 38 can be found at, for example, page 6, line 21 through page 7, line 23 in the specification. In addition, the specification, in the Examples at pages 31 through 46, contains sufficient disclosure

to teach one of skill in the art to practice the invention. In particular, the data in Figures 5 and 6, obtained from experiments described on pages 45 and 46, clearly demonstrate the efficacy of the claimed vaccine, i.e., the detection of antibodies against HpaA in the mucosal lining of the experimental rats. Therefore, contrary to the Examiner's contentions, the specification does enable any person skilled in the art of vaccines to make and use the invention commensurate in scope with the claim.

Claims 1-3, 9, 38, 43 and 44 have been rejected under 35 U.S.C.§ 112, second paragraph, as being indefinite for failing to distinctly claim the subject matter regarded as the invention. Claims 43 and 44 have been canceled. Therefore the rejection of these claims is now moot. Claims 1-3, 9 and 38 have been amended and, as amended, clearly define the invention as required by statute. Applicants request that the rejection be withdrawn.

Claim 1 has been rejected under 35 U.S.C. § 102(a) as being anticipated by Lee et al. (*Biochim. Biophys. Acta* 1371(2): 168-184, 1998). The Examiner has stated that this rejection can be overcome by submitting an English translation of the Swedish priority application No.9801288-3 filed on 14 April 1998. Accordingly, Applicants enclose a copy of the Swedish priority application in English, and request that the rejection be withdrawn.

Claim 1 has been rejected under 35 U.S.C. § 102(b) as being anticipated by Goldstein et al. (Chemistry and Physics of Lipids, 88(1): 21-36, 1997). According to the Examiner, Goldstein et al. disclose a method of producing a polymer particle for a vaccine delivery system as claimed. Applicants disagree.

Goldstein et al. do not disclose the claimed method. Goldstein et al. disclose a method for forming high-axial-ratio-microstructures (HARMs) for controlled release of drugs, wherein simply adding water to a solution of amphiphile (sphingolipids) in DMF while mixing brings about precipitation of the microstructures in a single step. The reference further discloses that individual amino acids such as N-acetyl-glycine and N-acetyl-proline can be used as components of the Goldstein amphiphiles instead of the sugar of the sphingolipid. However, There is no disclosure in Goldstein et al. that protein or even peptide antigens can be incorporated with particles for forming a vaccine delivery system.

The present method is one of producing a vaccine delivery system comprising a plurality of polymer particles wherein a water-insoluble protein antigen is incorporated with the polymer particles, the polymer particles comprising a matrix polymer. The present process further differs from that in Goldstein, in that the present polymer particles are formed by forming droplets of the W/O emulsion by dispersing the emulsion in a fluid medium, and removing the solvent from the organic O phase of the W/O emulsion in the presence of the solubilizing agent. In the process of Goldstein et al, the particles are recovered in the precipitate. Moreover, Goldstein does not disclose the use of a protein solubilizing agent as is in the claimed method. Furthermore, the vortexing step to which the Examiner refers is simply a mixing step and is not disclosed as a particle formation step as in the instant invention. Therefore, the reference of Goldstein et al. does not anticipate the claimed method, and Applicants request that the rejection be withdrawn.

Claims 1-3, 9 and 38 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Fountain et al. (U.S. Patent No. 4,610,868). The Examiner alleges that Fountain et al (U.S. Patent No. 4,610,868) disclose a process of producing polymer particles (lipid matrix carriers) for a vaccine or drug delivery system as claimed. Applicants disagree.

Fountain et al. do not disclose the claimed invention. The reference discloses lipid matrix carriers for sustained release of bioactive agents, which differ from the claimed polymer-particle-based delivery system. In fact, the Fountain disclosure of lipids is not a disclosure of polymers within the ordinary meaning of the term. The Fountain lipid matrix carriers are formed of lipids such as, cholesterol and sterols, which are described as "globular structures" formed by agitation of the phases before any removal of the solvent occurs. More particularly, the Examiner points to Fountain claim 51 as disclosing solvent removal. However, claim 50, from which 51 depends, recites that the "globular structures" are already formed by agitation of the phases prior to the removal of solvent recited in claim 51. In the present method (see step (b) of claim 1), the particles are formed by dispersion of the emulsion and with the removal of the solvent. Furthermore, Fountain et al. do not disclose that the particles are formed of polymers as claimed nor do they disclose use of a protein solubilizing agent. Therefore, Fountain et al. do not anticipate the claimed invention and Applicants request that the rejection be withdrawn.

The rejections of the claims under 35 U.S.C. § 102(e) and § 102(b) as being anticipated, respectively, by Maitra et al. (U.S. Patent No. 5,874,111) and Wu et al. (U.S. Patent No. 5,025,004) are now overcome in view of the amendments to the claims. According to the Examiner, these rejections were based on the 35 U.S.C. § 112, second paragraph. Since the claims now recite that the vaccine delivery system requires the presence of a water insoluble protein in the product produced by the method, the rejections should be withdrawn.

Claims 38-44 have been rejected under 35 U.S.C. §102(b) as being anticipated by Bölin et al. (WO 96/38475). In view of the cancellation of claims 39-44 and the amendment to claim 38, this rejection is now moot. Claim 38 now recites that the vaccine delivery system comprises a plurality of polymer particles, the polymer particles comprising a polymer matrix and a water insoluble protein antigen incorporated with the polymer particles. While Bölin et al. disclose the use of polymer microspheres as a suitable delivery system, they do not disclose that the vaccine delivery consists of polymer particles comprising a polymer matrix and a water insoluble protein incorporated with the polymer particles presently claimed. Therefore, the reference of Bölin et al. does not anticipate the claimed invention; the rejection should be withdrawn.

Claims 38-44 have been rejected under 35 U.S.C. §102(b) as being anticipated by Michael et al. (U.S. Patent No. 5,629,001). In view of the cancellation of claims 39-44 and the amendment to claim 38, this rejection is now moot. In addition, Michael et al. disclose an orally administrable therapeutic agent such as a protein, which is formulated by microencapsulating the therapeutic protein with an enteric coating under totally aqueous conditions without employing any nonaqueous solvents (see, e.g., col. 1, lines 66 through col. 2, lines 1-3). Claim 38 does not recite an enteric coat on the polymer particles. Accordingly, Michael et al. do not anticipate the claimed invention, and the rejection should be withdrawn.

Finally, Applicants acknowledge the Examiner's citation of the references of Czinn et al. (U.S. Patent No. 5,538,729), Buchel et al. (U.S. Patent No. 4,134,725), Chaiko et al. (U.S. Patent No. 5,948,263), Conte et al. (U.S. Patent No. 5,780,057), Elton et al. (U.S. Patent No. 5,104,904), Illig et al. (U.S. Patent No. 5,330,740), Martin et al. (U.S. Patent No. 4,344,934), Morrison et al. (U.S. Patent No. 5,827,531), Hunter et al. (U.S. Patent No. 5,622,649), WO 96/3631, WO 95/11010, WO 95/11009, Plaut et al. (U.S. Patent No. 5,334,544), WO 99/52550,

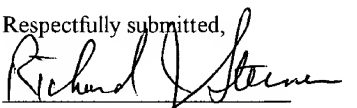
WO 96/40893 and Yager et al. (U.S. Patent No. 5,851,536). Applicants assert that none of these references, either alone or in combination, render obvious the claimed invention.

In view of the forgoing amendments and remarks, the claims are in condition for allowance. Reconsideration and allowance of the application are respectfully requested.

The Assistant Commissioner is hereby authorized to charge any required fees due for any reason to Deposit Account 23-1703.

Dated: May 24, 2001

Respectfully submitted,



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Version With Markings to Show Changes Made

In the Specification:

Last paragraph of page 12 (lines 27-30):

Other suitable techniques (modified anti-solvent (GAS) techniques) [sinclude] include: Precipitation with Compressed Anti-Solvents (PCA) procedure (Dixon *et al.*, *AIChE Journal*, **1993**, *39*, 127-139; and Supercritical Anti-Solvent (SAS) procedure (Yeo *et al.*, *Biotech.Bioeng.*, **1993**, *41*, 341-346) or Aerosol Solvent Extraction System (ASES) (DE744329).

See Specification pages 22, 23, 24 and 26 following for the marked-up versions of the additional paragraphs cited on pages 2-4 of this communication:

(1993) J. Bacteriol. 175, 674-683. Reference is also made to P W Toole *et al*, Bacteriology Vol. 177, No. 21, Nov. 1995; and Jones,A.C., Logan,R.P., Foynes,S., Cockayne,A., Wren,B.W. and Penn,C.W., J. Bacteriol. 179 (17), 5643-5647 (1997) which concern HpaA proteins.

The Hpa A protein is expressed by all *H. pylori* strains tested , and antibodies created towards this protein do not cross-react with common endogenous human bacteria of other species or with selected human tissues including the gastric mucosa. Thus being a well conserved putative adhesin with immunogenic properties, the HpaA protein is useful both for the detection of *H. pylori* infections as well as for the manufacture of vaccine compositions. Table 1 shows a comparison of HpaA amino acid sequences derived from 4 different strains of *H. Pylori*. It can be seen from the table that the sequence is highly conserved amongst different strains.

Table 1

Evans (8826)	MKTNGHFKDFAWKKCLLGTSVVALLVGCSPHIIETNEVALKLNYHPASEKVQALDEKILL	(SEQ ID NO:5)
GTC (J99)	MKTNGHFKDFAWKKCFLGASVVALLVGCSPHIIETNEVALKLNYHPASEKVQALDEKILL	(SEQ ID NO:6)
Trust (17874)	MKTNGHFKDFAWKKCLLGASVGALLVGCSPHIIETNEVALKLNYHPASEKVQALDEKILL	(SEQ ID NO:7)
Penn (11637)	MRANNHFKDFAWKKCLLGASVVALLVGCSPHIIETNEVALKLNYHPASEKVQALDEKILL	(SEQ ID NO:8)
TIGR (26695)	MRANNHFKDFAWKKCLLGASVVALLVGCSPHIIETNEVALKLNYHPASEKVQALDEKILL	(SEQ ID NO:9)
	:::.**********:**:** **********	
Evans (8826)	LRPAFQYSDNIAKEYENKFKNQTTLKVEEILQNQGYKVINVDSSDKDDFSFAQKKEGYLA	(SEQ ID NO:10)
GTC (J99)	LRPAFQYSDNIAKEYENKFKNQTTLKVEEILQNQGYKVINVDSSDKDDFSFAQKKEGYLA	(SEQ ID NO:11)
Trust (17874)	LRPAFQYSDNIAKEYENKFKNQTVLKVEQILQNQGYKVINVDSSDKDDFSFAQKKEGYLA	(SEQ ID NO:12)
Penn (11637)	LRPAFQYSDNIAKEYENKFKNQTALKVEQILQNQGYKVISVDSSDKDDFSFAQKKEGYLA	(SEQ ID NO:13)
TIGR (26695)	LRPAFQYSDNIAKEYENKFKNQTALKVEQILQNQGYKVISVDSSDKDDLSFSQKKEGYLA	(SEQ ID NO:14)
	*:********** **** ********** ******** *********	

Evans (8826)	VAMIGEIVLRPDPKRTIQKKSEPGLLFSTGLDKMEGVLIPAGFVKVTILEPMSGESLDSF	(SEQ ID NO:15)
GTC (J99)	VAMNGEIVLRPDPKRTIQKKSEPGLLFSTGLDKMEGVLIPAGFVKVTILEPMSGESLDSF	(SEQ ID NO:16)
Trust (17874)	VAMNGEIVLRPDPKRTIQKKSEPGLLFSTGLDKMEGVLIPAGFVKVTILEPMSGESLDSF	(SEQ ID NO:16)
Penn (11637)	VAMNGEIVLRPDPKRTIQKKSEPGLLFSTGLDKMEGVLIPAGFIKVTILEPMSGESLDSF	(SEQ ID NO:17)

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TIGR (26695)    VAMNGEIVLRPDPKRTIQKKSEPGLLFSTGLDKMEGVLIPAGFVKVTILEPMSGESLDSF (SEQ ID NO:16)
                *** ************************************:**************

Evans (8826)    TMDLSELDIQEKFLKTTHSSHSGGLVSTMVKGTDNSNDAIKSALNKIFASIMQEMDKKLT (SEQ ID NO:18)
GTC (J99)       TMDLSELDIQEKFLKTTHSSHSGGLVSTMVKGTDNSNDAIKSALNKIFASIMQEMDKKLT (SEQ ID NO:18)
Trust (17874)   TMDLSELDIQEKFLKTTHSSHSGGLVSTMVKGTDNSNDAIKSALNKIFGSIMQEIDKKLT (SEQ ID NO:19)
Penn (11637)    TMDLSELDIQEKFLKTTHSSHSGGLVSTMVKGTDNSNDAIKSALNKIFANIMQEIDKKLT (SEQ ID NO:20)
TIGR (26695)    TMDLSELDIQEKFLKTTHSSHSGGLVSTMVKGTDNSNDAIKSALNKIFANIMQEIDKKLT (SEQ ID NO:20)
                ************************************************..****:*****

Evans (8826)    QRNLESYQKDAKELKNKRNR (SEQ ID NO:21)
GTC (J99)       QRNLESYQKDAKELKNKRNR (SEQ ID NO:21)
Trust (17874)   QKNLESYQKDAKELKGKRNR (SEQ ID NO:22)
Penn (11637)    QKNLESYQKDAKELKGKRNR (SEQ ID NO:22)
TIGR (26695)    QKNLESYQKDAKELKGKRNR (SEQ ID NO:22)
                *:************.****
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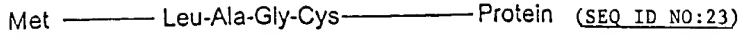
"*" at a certain position denotes an identical amino acid in all sequences

"." at a certain position denotes conserved amino acids (eg, amino acids of the same charge type such as lysine or arginine at a certain position).

Penn (11637)	DNA sequence deposited in Genbank under Accession No. X92502
Trust (17874)	DNA sequence deposited in Genbank under Accession No.U35455
Evans (8826)	DNA sequence deposited in Genbank under Accession No.X61574
TIGR (26695)	DNA sequence deposited under Accession No. AE000591
GTC (J99)	DNA sequence obtained in-house.

The strain names are indicated in brackets, strain 8826 being obtained from SWISS-PROT accession Q48264.

I 

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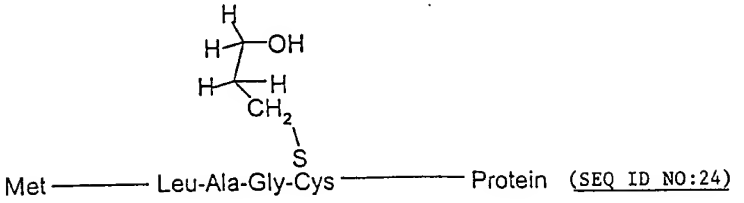
II 

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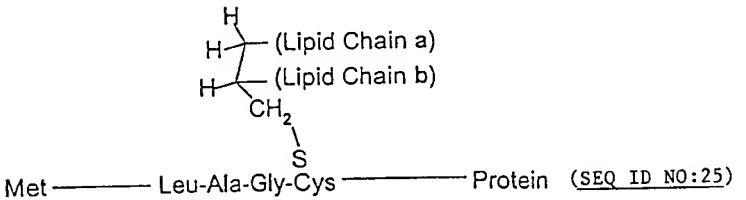
III 

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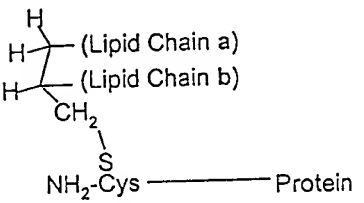
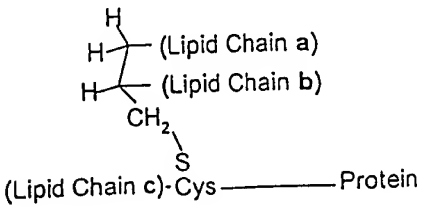
IV 

V 

In the Claims:

1. (Amended) A method for producing a vaccine delivery system comprising a plurality of polymer particles [for use as a vaccine delivery system in which], wherein a water insoluble protein antigen is incorporated with the polymer particles, the polymer particles comprising a [polymer] matrix polymer, wherein the method comprises:[-]

(a) mixing an aqueous phase (W) comprising the water insoluble protein and one or more solubilizing agents with an organic phase (O) that is immiscible with W to produce a W/O emulsion, [in which the water insoluble protein is solubilised in the W phase using a solubilizing agent, and] the O phase comprises the matrix polymer in an organic solvent;

(b) forming droplets of said W/O emulsion by dispersing the emulsion in a fluid medium, and removing said solvent from the O phase of the W/O emulsion droplets to thereby form the polymer particles incorporating the water insoluble protein antigen; and

wherein in step (a) [a stabilising agent is included] one or more stabilizing agents are provided in the W/O emulsion to stabilize the W/O emulsion in the presence of the solubilizing agent and promote the incorporation of the water insoluble protein with the polymer particles during step (b)[by stabilising the W/O emulsion in the presence of said solubilizing agent].

2. (Amended) The method of claim 1, wherein more than one [stabilising] stabilizing agent is included in the W/O emulsion.

3. (Amended) The method of claim 1 or 2, wherein the [or each stabilising] one or more stabilizing agents is/are selected from group consisting of polymers, polar lipids, and hydrophobic surfactants.

4. (Amended) The method of [any preceding] claim 3, wherein [a stabilising] the one or more stabilizing agents is/are [used that is] a polymer selected from the group consisting of poly(vinyl pyrrolidone), poly(vinyl alcohol), polysaccharides, polyethyleneoxide and water soluble proteins.

5. (Amended) The method of [any one of claims 1 to 3] claim 3, wherein [a stabilising] the one or more stabilizing agents [is used that] is/are a polar lipid selected from the group consisting of cholesterol, phosphatidylcholine, phosphatidylethanolamine, phosphatidylglycerol, glycolipids and phosphatidic acid.

6. (Amended) The method of[any one of claims 1 to 3] claim 3, wherein [a stabilising] the one or more stabilizing agents is/are [used that is] a non-ionic, hydrophobic surfactant selected from the group consisting of a sorbitan fatty acid ester, hydrophobic polyoxyethylene alkyl ether, sucrose ester, alkyl-glucopyranoside, polyglycerol polyricinoleate and block-copolymers of ethylene oxide with propyleneoxide and/or lactic acid.

7. (Amended) The method of [any one of claims 1 to 3] claim 3, wherein [a stabilising] the one or more stabilizing agents is/are [used that is] an anionic, hydrophobic surfactant selected from the group consisting of an alkylsulphate salt, a dialkylsulphosuccinate salt, an alkylbenzene sulphonate salt and a fatty acid salt.

8. (Amended) The method of [any one of claims 1 to 3] claim 3, wherein [a stabilising] the stabilizing agent is/are [used that is] a cationic, hydrophobic surfactant selected from the group consisting of an alkyltrimethylammonium salt and a dialkyldimethylammonium salt.

9. (Amended) The method of claim 2, wherein one of the stabilizing agents is a sorbitan fatty acid ester[is used as a stabilising agent].

10. (Amended) The method of claim 2, wherein the stabilizing agents comprise poly(vinyl pyrrolidone) and sodium 1, 4-bis(2-ethylhexyl) sulphosuccinate[are used as stabilising agents].

11. (Amended) The method of [any preceding] claim 1, wherein the aqueous phase comprises more than one [solubilizing agent is used] solubilizing agent.

12. (Amended) The method of [any preceding] claim 1, wherein the one or more solubilizing agents is/are a hydrophilic surfactant[is used as a solubilizing agent].

13. (Amended) The method of claim 12, wherein the hydrophilic surfactant is a non-ionic surfactant selected from the group consisting of alkyl-glucopyranosides, alkyl-thioglucopyranosides, alkyl-maltosides, alkoyl-methyl glucamides, glucamides, polyoxyethylene alcohols, polyoxyethylene alkyl phenols, emulphogens, polyoxyethylene sorbitol esters, polyoxyethylene fatty acid esters, hydrophilic polyoxyethylene alkyl ethers and digitonin.

14. (Amended) The method of claim 12, wherein the hydrophilic surfactant is an anionic surfactant selected from the group consisting of cholates, alkylsulphonates, deoxycholates, alkylsulphates, oligooxyethylene dodecyl ether sulphates and sodium dodecylsarcosinate.

15. (Amended) The method of claim 12, wherein the hydrophilic surfactant is a cationic surfactant selected from the group consisting of alkylpyridinium salts and alkyltrimethylammonium salts.

16. (Amended) The method of claim 12, wherein the hydrophilic surfactant is a zwitterionic surfactant selected from the group consisting of (3-[(3-cholamidopropyldimethylammonio]-1-propanesulphonate) (CHAPS), (3-[(3-cholamidopropyl)-dimethylammonio]-2-hydroxy-1-propanesulphonate) (CHAPSO), (N,N-*bis*[3-D-gluconamidopropyl]-cholamide) (BIGCHAP),

(N,N-bis[3-D-gluconamidopropyl]-deoxycholamide) (deoxy BIGCHAP), lyso phosphatidylcholine, alkylbetaines and sulphobetaines.

17. (Amended) The method of [any one of claims 1 to 11] claim 1, wherein the one or more solubilizing agents is/are a chaotropic agent[is used as a solubilizing agent].

18. (Amended) The method of claim 17, wherein the chaotropic agent is selected from the group consisting of a perchlorate, thiocyanate, guanidine, chlorate, iodide, bromide, nitrate and urea.

19. (Amended) The method of [any preceding] claim 1, wherein the method is a Double Emulsion (W/O/X) Solvent Evaporation Technique[for producing polymer particles for use as a vaccine delivery system, in which] and in step (b) the [stabilised] stabilized W/O emulsion is dispersed in a liquid phase (X) which is immiscible with the O phase to produce a W/O/X double emulsion comprising W/O droplets from which the solvent is evaporated[, thereby producing said polymer particles incorporating the water insoluble protein antigen].

20. (Amended) The method of [any one of claims 1 to 18] claim 1, wherein the method is a Double Emulsion (W/O/X) Solvent Extraction Technique[for producing polymer particles for use as a vaccine delivery system, in which] and in step (b) the [stabilised] stabilized W/O emulsion is dispersed in a liquid phase (X) which is immiscible with the O phase to produce a W/O/X double emulsion comprising W/O droplets, wherein the X phase extracts said solvent from the O phase of the droplets[, thereby producing said polymer particles incorporating the water insoluble protein antigen].

21. (Amended) The [technique] method of claim 19 or 20, wherein [a stabilising agent is included in] the X phase comprises a stabilizing agent.

22. (Amended) The [technique] method of claim 21, wherein [a stabilising agent as defined in any one of claims 3 to 8 is used in the X phase] the one or more stabilizing agents is/are selected from group consisting of polymers, polar lipids, and hydrophobic surfactants.

23. (Amended) The method of [any one of claims 1 to 18] claim 1, wherein the method is a spray drying technique [for producing polymer particles for use as a vaccine delivery system, in which], and in step (b) the [stabilised] stabilized W/O emulsion is dispersed in a gaseous medium to form a spray of W/O emulsion droplets from which said solvent evaporates[, thereby producing said polymer particles incorporating the water insoluble protein antigen].

24. (Amended) The method of [any one of claims 1 to 18] claim 1, wherein [in] step (b) comprises a fluid gas technique[is used] to form the polymer particles.

25. (Amended) The method of claim 24, wherein the fluid gas technique is selected from the group consisting of gas anti-solvent precipitation (GAS), solution enhanced dispersion by supercritical fluid (SEDS), precipitation with compressed anti-solvents (PCA), supercritical anti-solvent (SAS) and aerosol solvent extraction system (ASES).

26. (Amended) The method of [any preceding] claim 1, wherein the protein antigen is a *Helicobacter* protein or *Helicobacter* protein fragment[thereof].

27. (Amended) The method of claim 26, wherein the [protein antigen] *Helicobacter* protein or *Helicobacter* protein fragment [thereof] is from [a] *Helicobacter pylori* [protein or fragment thereof].

29. (Amended) The method of claim 28, wherein the *Helicobacter* protein is a lipidated form of *Helicobacter pylori* adhesion antigen (HpaA).

32. (Amended) The method of [any preceding] claim 1, wherein the matrix polymer is a homo-or co-polymer selected from one or more of the group consisting of polyesters, polyanhydrides, polyorthoesters, polycarbonates, polyamides, poly(amino acids), polyacetals, polycyanoacrylates, polyacrylates, biodegradable polyurethanes, non-erodable polyurethanes, polymers of ethylene-vinyl acetate, acyl substituted cellulose acetates, polysaccharides, polystyrenes, polyvinyl chloride, polyvinyl fluoride, poly(vinyl imidazole), chlorosulphonated polyolefins, polyethylene oxide, polyethers and polyoxalates.

33. (Amended) The method of claim 32, wherein the matrix polymer is a polyester homopolymer selected from the group consisting of polylactic acid, polyglycolic acid, polyhydroxybutyrate, poly(alpha hydroxyacids) and polycaprolactone.

34. (Amended) The method of claim 32, wherein the matrix polymer is a polyester co-polymer selected from the group consisting of poly(lactide-co-glycolide), poly(lactic-co-glycolic acid), poly(hydroxybutyrate-hydroxyvalerate) and poly(lactide-co-caprolactone).

36. (Amended) The method of [any preceding] claim 1, wherein in step (a) the W phase is mixed with the O phase in a ratio by volume of 1:100 to 1:1.

37. (Amended) A [polymer particle] vaccine delivery system [obtainable] produced by the method of [any preceding] claim 1, wherein the one or more stabilizing agents is/are a polymer selected from the group consisting of poly(vinyl pyrrolidone), poly(vinyl alcohol), polysaccharides, polyethyleneoxide and water soluble proteins, and the method is a Double Emulsion (W/O/X) Solvent Evaporation Technique and in step (b) the stabilized W/O emulsion is dispersed in a liquid phase (X) which is immiscible with the O phase to produce a W/O/X double emulsion comprising W/O droplets from which the solvent is evaporated.

38. (Amended) A [polymer particle]vaccine delivery system [in which] comprising a plurality of polymer particles, the polymer particles comprising a polymer matrix and a water insoluble protein antigen [is] incorporated with the polymer particles[comprising a polymer matrix].

45. (Amended) The vaccine delivery system of [any one of claims 38 to 44] claim 38, wherein the matrix polymer is a homo- or co-polymer selected from one or more of the group consisting of polyesters, polyanhydrides, polyorthoesters, polycarbonates, polyamides, poly(amino acids), polyacetals, polycyanoacrylates, polyacrylates, biodegradable polyurethanes, non-erodable polyurethanes, polymers of ethylene-vinyl acetate, acyl substituted cellulose acetates, polysaccharides, polystyrenes, polyvinyl chloride, polyvinyl fluoride, poly(vinyl imidazole), chlorosulphonated polyolefins, polyethylene oxide, polyethers and polyoxalates.

46. (Amended) The vaccine delivery system of claim 45, wherein the polymer is a polyester homopolymer selected from the group consisting of polylactic acid, polyglycolic acid, polyhydroxybutyrate, poly(alpha hydroxyacids) and polycaprolactone.

47. (Amended) The vaccine delivery system of claim 45, wherein the matrix polymer is a polyester co-polymer selected from the group consisting of poly(lactide-co-glycolide), poly(lactic-co-glycolic acid), poly(hydroxybutyrate-hydroxyvalerate) and poly(lactide-co-caprolactone).

49. (Amended) The vaccine delivery system of any one of claims [37 to 48] 37, 38 and 45-48 , wherein the polymer particles have an average diameter of 0.05-20 μm according to the volume size distribution.

50. (Amended) A vaccine composition comprising the vaccine delivery system of any one of claims [37 to 49] 37, 38, and 45-49.

51. (Amended) [Use of the delivery system of any one of claims 37 to 49 in the manufacture of a vaccine composition,] A method for the treatment of *Helicobacter* infection in a mammalian host, comprising administering to the mammalian host an effective amount of the vaccine composition according to claim 50.

52. (Amended) [Use of the delivery system of any one of claims 37 to 49 in the manufacture of a vaccine composition,] A method for preventing or reducing the risk of *Helicobacter* infection in a mammalian host, comprising administering to the mammalian host an effective amount of the vaccine composition according to claim 50.

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Notice of Non-Compliant Amendment (37 CFR 1.121)

The amendment filed on 4/09/01 is considered non-compliant because it has not been submitted in the format required under **37 CFR 1.121**, as amended on September 8, 2000 (see 65 Fed. Reg. 54603, Sept. 8, 2000 and 1238 O.G. 77, Sept. 19, 2000).

- ☑ The amendment does not include a clean version of the **replacement paragraph/section**. 37 CFR 1.121(b)(1)(ii)
- ☑ The amendment does not include a marked-up version of the **replacement paragraph/section** 37 CFR 1.121(b)(1)(iii)
- ☑ The amendment does not include a clean version of the **amended claim(s)**. 37 CFR 1.121(c)(1)(i)
- ☑ The amendment does not include a marked-up version of the **amended claim(s)**. 37 CFR 1.121(c)(1)(ii)

For your convenience, attached to this correspondence is a copy of an informational flyer (MPEP Bookmark Bulletin on "Simplified Amendment Practice").

Applicant is given a TIME PERIOD of **ONE (1) MONTH** or **THIRTY (30) DAYS** from the mailing date of this notice, whichever is longer, within which to submit an amendment in compliance with 37 CFR 1.121, effective March 1, 2001, in order to avoid abandonment. EXTENSIONS OF THIS TIME PERIOD MAY BE GRANTED UNDER 37 C.F.R. 1.136(a).

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